

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method of modulating mammalian smooth muscle cell activity, said method comprising modulating the functional activity of sphingosine kinase mediated signalling wherein upregulating sphingosine kinase mediated signalling to a functionally effective level upregulates said smooth muscle cell activity and downregulating sphingosine kinase mediated signalling to a functionally ineffective level downregulates said smooth muscle cell activity.

2. (Original) A method of regulating smooth muscle cell activity in a mammal, said method comprising modulating the functional activity of sphingosine kinase mediated signalling in said mammal wherein upregulating sphingosine kinase mediated signalling activity to a functionally effective level upregulates said smooth muscle cell activity and downregulating sphingosine kinase mediated signalling to a functionally ineffective level downregulates said smooth muscle cell activity.

3. (Original) A method for the treatment and/or prophylaxis of a condition characterised by aberrant, unwanted or otherwise inappropriate smooth muscle cell activity in a mammal, said method comprising modulating the functional activity of sphingosine kinase mediated signalling wherein upregulating sphingosine kinase mediated signalling to a functionally effective level upregulates said smooth muscle cell activity and downregulating sphingosine kinase mediated signalling to a functionally ineffective level downregulates said smooth muscle cell activity.

4. (Original) The method according to claim 1 or 2 or 3 wherein said smooth muscle cell is a vascular, bronchial or intestinal smooth muscle cell.

5. (Original) The method according to claim 4 wherein said vascular smooth muscle cell is an arterial smooth muscle cell.

6. (Original) The method according to claim 1 or 2 or 3 wherein said smooth muscle cell is a gastric, bladder or uterine smooth muscle cell.

7. (Currently Amended) The method according to ~~any one of claims 1 to 6~~ claim 1 or 2 or 3 wherein said smooth muscle cell activity is smooth muscle cell tone.

8. (Original) The method according to claim 7 wherein said smooth muscle cell is a bronchial smooth muscle cell and said modulation of bronchial smooth muscle cell tone is downregulation of tone.

9. (Original) The method according to claim 7 wherein said smooth muscle cell is a vascular smooth muscle cell and said modulation of vascular smooth muscle cell tone is downregulation of tone.

10. (Original) The method according to claim 7 wherein said smooth muscle cell is a vascular smooth muscle cell and said modulation of vascular smooth muscle cell tone is upregulation of tone.

11. (Original) The method according to claim 3 wherein said condition is excessive arterial resistance, said smooth muscle cell activity is arterial smooth muscle cell tone and said modulation of sphingosine kinase activity is downregulation of activity.

12. (Original) The method according to claim 11 wherein said condition is high blood pressure.

13. (Original) The method according to claim 12 wherein said high blood pressure correlates to hypertension.

14. (Original) The method according to claim 3 wherein said condition is inadequate arterial resistance, said smooth muscle cell activity is arterial smooth muscle cell tone and said modulation of sphingosine kinase activity is upregulation of activity.

15. (Original) The method according to claim 14 wherein said condition is hypotension or septic shock.

16. (Original) The method according to claim 15 wherein said hypotension is related to Waterhouse-Friedrichsen syndrome.

17. (Original) The method according to claim 15 wherein said septic shock is related to bacterial meningitis.

18. (Original) The method according to claim 3 wherein said condition is excessive bronchial constriction, said smooth muscle cell activity is bronchial smooth muscle cell tone and said modulation of sphingosine kinase activity is downregulation.

19. (Original) The method according to claim 18 wherein said excessive bronchial constriction is related to asthma, allergy or anaphylactic shock.

20. (Currently Amended) The method according to claim 1 or 2 or 3~~any one of claims 1-7, 10 or 14-17~~ wherein said modulation is upregulation of sphingosine kinase mediated signalling and said upregulation is achieved by introducing into said smooth muscle

cell a nucleic acid molecule encoding sphingosine kinase or functional equivalent, derivative or homologue thereof or the sphingosine kinase expression product or functional derivative, homologue, analogue, equivalent or mimetic thereof.

21. (Currently Amended) The method according to claim 1 or 2 or 3~~any one of claims 1-19~~ wherein said modulation is achieved by contacting said smooth muscle cell with a proteinaceous or non-proteinaceous molecule which modulates transcriptional and/or translational regulation of the sphingosine kinase gene.

22. (Currently Amended) The method according to claim 1 or 2 or 3~~any one of claims 1-7, 10 or 14-17~~ wherein said modulation is upregulation of sphingosine kinase levels and said upregulation is achieved by contacting said smooth muscle cell with a proteinaceous or non-proteinaceous molecule which functions as an agonist of the sphingosine kinase expression product.

23. (Currently Amended) The method according to claim 1 or 2 or 3~~any one of claims 1-9, 11-13 or 18-19~~ wherein said modulation is downregulation of sphingosine kinase mediated signalling and said downregulation is achieved by contacting said smooth muscle cell with a proteinaceous or non-proteinaceous molecule which functions as an antagonist to the sphingosine kinase expression product.

24. (Original) The method according to claim 23 wherein said molecule is a mutant sphingosine kinase which mutant is characterised by substitution of the glycine residue at position 82 to aspartate.

25. (Original) The method according to claim 1 wherein said smooth muscle cell activity is modulated *in vivo*.

26. (Original) The method according to claim 1 wherein said smooth muscle cell activity is modulated *in vitro*.

27. (Original) Use of an agent capable of modulating the functionally effective level of sphingosine kinase mediated signalling in the manufacture of a medicament for the regulation of vascular smooth muscle cell activity in a mammal wherein upregulating sphingosine kinase mediated signalling to a functionally effective level upregulates said smooth muscle cell activity and downregulating sphingosine kinase mediated signalling to a functionally ineffective level downregulates said smooth muscle cell activity.

28. (Original) Use of an agent capable of modulating the functionally effective level of sphingosine kinase mediated signalling in the manufacture of a medicament for the treatment of a condition characterised by aberrant, unwanted or otherwise inappropriate smooth muscle cell activity in a mammal wherein upregulating sphingosine kinase mediated signalling to a functionally effective level upregulates said smooth muscle cell activity and downregulating sphingosine kinase mediated signalling to a functionally ineffective level downregulates said smooth muscle cell activity.

29. (Original) Use according to claim 27 or 28 wherein said smooth muscle cell is a vascular, bronchial or intestinal smooth muscle cell.

30. (Original) Use according to claim 29 wherein said vascular smooth muscle cell is an arterial smooth muscle cell.

31. (Original) Use according to claim 27 or 28 wherein said smooth muscle cell is a gastric, bladder or uterine smooth muscle cell.

32. (Currently Amended) Use according to claim 27 or 28any one of claims ~~27-34~~ wherein said smooth muscle cell activity is smooth muscle cell tone.

33. (Original) Use according to claim 32, wherein said smooth muscle cell is a bronchial smooth muscle cell and said modulation of bronchial smooth muscle cell tone is downregulation of tone.

34. (Original) Use according to claim 32 wherein said smooth muscle cell is a vascular smooth muscle cell and said modulation of vascular smooth muscle cell tone is downregulation of tone.

35. (Original) Use according to claim 32 wherein said smooth muscle cell is a vascular smooth muscle cell and said modulation of vascular smooth muscle cell tone is upregulation of tone.

36. (Original) Use according to claim 28 wherein said condition is excessive arterial resistance, said smooth muscle cell activity is arterial smooth muscle cell tone and said modulation of sphingosine kinase activity is downregulation of activity.

37. (Original) Use according to claim 36 wherein said condition is high blood pressure.

38. (Original) Use according to claim 37 wherein said high blood pressure correlates to hypertension.

39. (Original) Use according to claim 28 wherein said condition is inadequate arterial resistance, said smooth muscle cell activity is arterial smooth muscle cell tone and said modulation of sphingosine kinase activity is upregulation of activity.

40. (Original) Use according to claim 39 wherein said condition is hypotension or septic shock.

41. (Original) Use according to claim 40 wherein said hypotension is related to Waterhouse-Friedrichsen syndrome.

42. (Original) Use according to claim 40 wherein said septic shock is related to bacterial meningitis.

43. (Original) Use according to claim 28 wherein said condition is excessive bronchial constriction, said smooth muscle cell activity is bronchial smooth muscle cell tone and said modulation of sphingosine kinase activity is downregulation.

44. (Original) Use according to claim 43 wherein said excessive bronchial constriction relates to asthma, allergy or anaphylactic shock.

45. (Currently Amended) Use according to claim 27 or 28~~any one of claims 27-32, 35 or 39-42~~ wherein said modulation is upregulation of sphingosine kinase mediated signalling and said upregulation is achieved by introducing into said smooth muscle cell a nucleic acid molecule encoding sphingosine kinase or functional equivalent, derivative or homologue thereof or the sphingosine kinase expression product or functional derivative, homologue, analogue, equivalent or mimetic thereof.

46. (Currently Amended) Use according to claim 27 or 28~~any one of claims 27-44~~ wherein said modulation is achieved by contacting said smooth muscle cell with a proteinaceous or non-proteinaceous molecule which modulates transcriptional and/or translational regulation of the sphingosine kinase gene.

47. (Currently Amended) Use according to claim 27 or 28~~any one of claims 27-32, 35 or 39-42~~ wherein said modulation is upregulation of sphingosine kinase levels and said upregulation is achieved by contacting said smooth muscle cell with a proteinaceous or non-

proteinaceous molecule which functions as an agonist of the sphingosine kinase expression product.

48. (Currently Amended) Use according to ~~claim 27 or 28~~^{any one of claims 27-34, 36-38 or 43-44} wherein said modulation is downregulation of sphingosine kinase mediated signalling and said downregulation is achieved by contacting said smooth muscle cell with a proteinaceous or non-proteinaceous molecule which functions as an antagonist to the sphingosine kinase expression product.

49. (Original) Use according to claim 48 wherein said molecule is a mutant sphingosine kinase which mutant is characterised by substitution of the glycine residue at position 82 to aspartate.

50. (Original) Use according to claim 27 wherein said smooth muscle cell activity is modulated *in vivo*.

51. (Original) Use according to claim 27 wherein said smooth muscle cell activity is modulated *in vitro*.

52. (Original) A pharmaceutical composition comprising the modulatory agent as hereinbefore defined and one or more pharmaceutically acceptable carriers and/or diluents.